Several controversies will undoubtedly arise with the adoption of the IASLC staging system.

In the current UICC-6 system, T4 lesions are staged as IIIB regardless of lymph node status and are considered unresectable except in special circumstances. In this study, shifting of stage with application of the IASLC may potentially alter the management of 134 (11.6%) patients. Sixty-three of these patients were upstaged from a stage where surgery alone is the recommended treatment to a stage where adjvant chemotherapy may be considered.[13-15] Additionally, 10 patients were upstaged to a stage where neoadjuvant chemotherapy is frequently offered (stage II to IIIA). The role of adjuvant and neoadjuvant chemotherapy in these patient populations may need to be re-evaluated. The IASLC system T4 lesions would be considered as IIIA or IIIB and the designation is based on the presence of absence of mediastinal nodal metastases. Satellite nodules in the ipsilateral primary lobe are considered unresectable T4 (stage IIIB) disease by UICC-6 criteria but T3 (stage IIB or IIIA) and potentially resectable by IASLC. Additionally, a satellite nodule in the ipsilateral lung but outside the primary lobe is unresectable M1 (stage IV) in the UICC-6 system and potentially resectable T4 (stage IIIA or IIIB) by IASLC. The optimal treatment strategy for these stages needs to be re-evaluated. Further study and validation of IASLC staging system and its effects on patient care are warranted.

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Discussion

Dr Bryan Fitch Meyers *(St. Louis, Mo).* I congratulate Dr Kassis on his presentation. Because there were not any photographs of aortas or mitral valves, I am going to use some of my time to underscore some of his findings and elaborate a little bit, then follow up with two short questions.

First of all, the old system was created using 5000 patients, 90% of them from a single center, M. D. Anderson, where Dr Kassis is working right now. The new system was created using morethan 100,000 patients collected worldwide, and it really is an international effort to represent uniform staging for patients with lung cancer. Twenty-eight thousand of those patients actually had a thoracotomy. This major revision has expanded the ability to make clear statements about staging.

If we assume that these proposed changes are meaningful and important changes based on 28,000 operated patients, then what conclusions would be drawn on the basis of the results of a confirmatory study like this? First, we would either be reassured or raise some doubt that the M. D. Anderson method of selecting patients and treating patients is consistent with those done in the rest of the world. If we assume that the M. D. Anderson system is representative of North America or American techniques, if these results were discrepant with the findings of the international group, we would wonder whether North America or America is distinct from other groups. Fortunately, your results are reassuring in that they confirm the recommendations by the international group.

It turns out that the findings that interest us most in a staging system are three things. What we want to see when one makes a change in a staging system, particularly a long awaited change like this, is that patients do shift from one stage to another. Dr Kassis has mentioned that 17% of the patients were shifted from one stage to another, and whether you use a *P* value or not, that is a substantial and clinically important change in the way that patients were assigned a stage. That number in itself tells us this was a meaningful change. The other aspects that are important are the distinctiveness of the stage groups and the heterogeneity within each stage group.

If you look at Dr Kassis' slide of the old system, with the stage IIA curve crossing over the IIB and then crossing over the IB, there is deficiency in the distinctiveness of the curves. However, if you move to the next slide where they applied the new staging system to their own data, you see that that distinctiveness has been improved with the new system. So, again, his presentation shows the superiority of the new system.

One area that was lacking in your presentation and discussion pertains to the problem of heterogeneity within each stage group. Is there a way that you could add to these results that reassures us that the patients who moved were moved from a group where they were less representative to a group that they now are more representative and homogeneous in their new stage group?

Dr Kassis. We did not definitively look at heterogeneity between stages, although that is a very good question and something that we could certainly evaluate at a future time. What we did do, though, is attempt to look at Kaplan–Meier curves in terms of stratifying these patients based on their ability to differentiate patients on the basis of stage. We took it one step further to try and do a statistical assessment of these patients by using a model called the permutation test to help quantify the differences that we see based on the Kaplan–Meier curve. However, your question regarding heterogeneity is something that we need to look at in the future.

Dr Meyers. The other question I had for you is that when we do a model, either a predictive or a descriptive model, and we want to validate it, we often use cases that were not used to create the model, and this was not mentioned in your presentation or the paper. Did the M. D. Anderson patients who were presented here play a role in the 28,000 operated patients who were used to create this new model? What are your thoughts on the impact of your answer on the importance of these results?

Dr Kassis. Less than 10% of our patient population of the 1154 patients was analyzed by the IASLC system, and the length of follow-up was such that in our estimation they are two completely separate data sets.

Dr Frank C. Detterbeck *(New Haven, Conn).* I just have a comment. I think that we need to be careful about what we are trying to get from this. There are many purposes to a staging system. One is to have a nomenclature so that when one person is talking about certain patients in one study and another person is talking about them in another institution, the same group of patients are being discussed. Another is to determine prognosis, and that is clearly what was chosen as the primary goal in the IASLC staging project. And clearly it meets that goal. I think a third one, which is to select appropriate treatment for patients, is a bit of a slippery slope. That is not what the IASLC staging project was designed to do and it is not what staging systems are designed to do. Now, we use the language to help us talk about it, but it is really clinical trials that define what the appropriate treatment is for patients. We cannot just identify a stage (eg, stage II) and base treatment merely on that. We have to look at which patients we are talking about and what the clinical trials have shown us that we should be doing.

I think that you are taking the stage classification system to a different realm here than what it was intended to do, and I am not sure that that is really appropriate.

Dr Kassis. Thank you for your comments. I do agree with you. I do not think that we should be altering patient management on the basis of the stage shifting that we have demonstrated here. What I am trying to demonstrate is that the shifting of patients may lead to further studies so that we can better assess and better determine what to do with these patients with a satellite nodule in the ipsilateral lobe that was formerly T4 in stage IIIB disease. In the current system, if they are N0, they are going to be stage IIB; if they are N1, they are going to be stage IIIA. I think we need further studies to evaluate how we are going to manage these patients now that are assigned different stage groupings.